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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/725,079	12/02/2003	Peng Cho Tang	034536-0904	2712

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EXAMINER	
BALASUBRAMANIAN, VENKATARAMAN	

ART UNIT	PAPER NUMBER
1624	

DATE MAILED: 09/10/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/725,079	TANG ET AL.	
	Examiner	Art Unit	
	Venkataraman Balasubramanian	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 June 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-37* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-37* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group I, claims 1-9, 18 in the reply filed on 6/3/2004 is acknowledged.

In view of applicants' response, which indicates an error in the Election/Restriction made by the previous office action and upon further consideration, the restriction requirement made in the previous office action is withdrawn.

Claims 1-37 are now under examination.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-37 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Following reasons apply. Any claim not specifically rejected is rejected as being dependent on a rejected claim and share the same limitation

1. Recitation of "C-amido" in the definition of R^1 in claim 1, renders the claim 1 indefinite as the term "C-amido" is ambiguous. First of all, it is not clear whether the term to treated as an $CONH_2$ group with the nitrogen unsubstituted or to include N-substituted group. Secondly the C-amido appears to specify link through CO of the amide but it is appended to nitrogen of the indolinone ring. How can such a group be C-amido? Note this group appears at various variable

group definition and hence renders claim 1 and other dependent claims indefinite.

2. Recitation of "sulfonyl" in the definition of R^1 in claim 1, renders the claim indefinite as the "sulfonyl" group is a divalent group and what is appended to the free valence of the group is not defined.

3. Similarly, recitation of "sulfinyl", "sulfonyl" or "sulfonamido "in the definition of R^3, R^4, R^5 and R^6 in claim 1, renders the claim indefinite as these groups are divalent group and what is appended to the free valence of the group is not defined. See also recitation of "carbonyl" group. What is appended to the free valence of this divalent group also remains unknown.

4. Recitation of the term "prodrug" in the claim 1 is deemed as indefinite. Prodrugs in general and as noted in specification, are compounds, which undergo in vivo hydrolysis to parent active drugs. These include esters, carbamates, alkoxy carbonyls etc. In that sense recitation of prodrug is acceptable. However, the claim includes such groups, namely ester, and amide and therefore it is not clear what is the difference between these variable groups and the prodrug group.

In addition, it is not clear whether compounds bearing the said ester and or amide groups are excluded from being potential "prodrug". If compounds bearing these groups, which are likely to undergo in vivo transformation, is excluded then what is included in the definition of prodrug and where on the compound of formula shown in claim 1, these groups are placed, is not clear. Note the same term occurs in claims 10 and 18.

In addition claim 10 includes prodrug for a method of use to modulate kinase activity, which is confusing as prodrugs are supposed to inactive as is but undergoes transformation to active drug. It is not clear how would one be able to use prodrug in this method of use.

5. In claim 9, which recites "selected from the group consisting of", an "and" is missing at various places before the last choices of the variable recited therein.

6. Recitation of "comprises" in claims 11, 12, 14, 16, 20, 21, 23, 25, 28, 30, 31, 32, 34 and 35, renders these claims indefinite as the transitional phrase "comprises" is open-ended and can include more than what is being positively recited therein. See MPEP 2111.03 which states: The transitional term "comprising", which is synonymous with "including," "containing," or"characterized by," is inclusive or open-ended and does not exclude additional, unrecited elements or method steps. See, e.g., Genentech, Inc. v. Chiron Corp., 112 F.3d 495,501, 42 USPQ2d 1608, 1613 (Fed. Cir. 1997) ("Comprising" is a term of art used in claim language which means that the named elements are essential, but other elements may be added and still form a construct within the scope of the claim.); Moleculon Research Corp. v. CBS, Inc., 793 F.2d 1261, 229 USPQ 805 (Fed. Cir. 1986); In re Baxter, 656 F.2d 679, 686, 210 USPQ 795, 803 (CCPA 1981); Ex parte Davis, 80 USPQ 448, 450 (Bd. App. 1948) ("comprising" leaves "the claim open for the inclusion of unspecified ingredients even in major amounts"). Replacement of "comprises" with "is" is suggested.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-37 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for salts of the claimed compounds, does not reasonably provide enablement for making prodrugs of the claimed compounds. The claim(s) contains subject matter that was not described in the specification in such a way as to enable one skilled in the art of medicinal chemistry - to use the invention. . Any claim not specifically rejected is rejected as being dependent on a rejected claim and share the same limitation

"The factors to be considered in making an enablement rejection have been summarized as the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in that art, the predictability or unpredictability of the art and the breadth of the claims", In re Rainer, 146 USPQ 218 (1965); In re Colianni, 195 USPQ 150, Ex parte Formal, 230 USPQ 546. a) Finding a prodrug is an empirical exercise. Predicting if a certain ester of a claimed alcohol, for example, is in fact a prodrug, and produces the active compound metabolically, in man, at a therapeutic concentration and at a useful rate is filled with experimental uncertainty. Although attempts have been made to predict drug metabolism 'de novo, this is still an experimental science. For a compound to be a prodrug, it must meet three tests. It must itself be biologically inactive. It must be metabolized to a second substance in a human at a rate and to an extent to produce that second substance at a physiologically

meaningful concentration. Thirdly, that second substance must be biologically active. Thus, determining whether a particular compound meets these three criteria in a clinical trial setting requires a large quantity of experimentation.

b) The direction concerning the prodrugs is found in the passage spanning line 32, page 12 to line 11, page 13. c) There is no working example of a prodrug of a compound the formula (I). d) The nature of the invention is clinical use of compounds and the pharmacokinetic behavior of substances in the human body. e) The state of the prodrug art is summarized by Wolff (Medicinal Chemistry). The table on the left side of page 976 outlines the research program to be undertaken to find a prodrug. The second paragraph in section 10 and the paragraph spanning pages 976-977 indicate the low expectation of success. In that paragraph the difficulties of extrapolating between species are further developed. Since, the prodrug concept is a pharmacokinetic issue, the lack of any standard pharmacokinetic protocol discussed in the last sentence of this paragraph is particularly relevant. Banker (Modem Pharmaceutics) in the first sentence, third paragraph on page 596 states that "extensive development must be undertaken" to find a prodrug. I) Wolff (Medicinal Chemistry) in the last paragraph on page 975 describes the artisans making Applicants' prodrugs as a collaborative team of synthetic pharmaceutical chemists and metabolism experts. All would have a Ph. D. degree and several years of industrial experience. g) It is well established that "the scope of enablement varies inversely degree of unpredictability of the factors involved", 'and physiological activity is generally considered to be an unpredictable factor. See In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). h) The breadth of the

claims includes all of the hundreds of thousands of compounds of formula of claim I as well as the presently unknown list of potential prodrug derivatives embraced by the word "prodrug".

Thus, undue experimentation will be required to determine if any particular derivative is, in fact, a prodrug.

MPEP 2164.01(a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. In re Wright, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here. Thus, undue experimentation will be required to make Applicants' invention.

Claims 10-17 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for modulation of few kinases shown in pages 101-16O of the specification, does not reasonably provide enablement for modulation of any or all receptor or non-receptor protein kinases generically embraced in claim language and protein kinase modulation by prodrugs of the claimed compounds. The claim(s) contains subject matter that was not described in the specification in such a way as to enable one skilled in the art of medicinal chemistry - to use the invention. . Any claim not specifically rejected is rejected as being dependent on a rejected claim and share the same limitation

The instant claims are drawn to modulation of any or all protein kinases including those specifically recited in the claims in general for which there is no enabling disclosure. Reading specification it appears that because of the specific assays recited for specific kinases, applicants' are asserting that instant compounds and their prodrug would be useful for modulating any or all protein kinases. But specification does not provide support for such an assertion. A single class of compound can modulate an entire genus of protein kinases is an incredible finding for specification lacks adequate enabling disclosure.

Furthermore, the instant claims recite modulation of protein kinases by prodrugs as well. As noted above, prodrugs are inactive compound and it is not clear how they would modulate the kinase activity. Note substantiation of utility and its scope is required when utility is "speculative", "sufficiently unusual" or not provided. See Ex parte Jovanovics, 211 USPQ 907, 909; In re Langer 183 USPQ 288. Also note Hoffman v. Klaus 9 USPQ 2d 1657 and Ex parte Powers 220 USPQ 925 regarding type of testing needed to support in vivo uses.

Next, applicant's attention is drawn to the Revised Interim Utility and Written Description Guidelines, at 64 FR 71427 and 71440 (December 21, 1999) wherein it is emphasized that 'a claimed invention must have a specific and substantial utility'. The disclosure in the instant case is not sufficient to enable the instantly claimed method of modulation of any or all protein kinases by parent compound or its prodrug solely based on the inhibitory activity disclosed for the compounds. The state of the art is indicative of the requirement for undue experimentation.

In evaluating the enablement question, several factors are to be considered. Note *In re Wands*, 8 USPQ2d 1400 and *Ex parte Forman*, 230 USPQ 546. The factors include: 1) The nature of the invention, 2) the state of the prior art, 3) the predictability or lack thereof in the art, 4) the amount of direction or guidance present, 5) the presence or absence of working examples, 6) the breadth of the claims, and 7) the quantity of experimentation needed.

1) The nature of the invention: Method of use of the compounds in modulation protein kinases in general.

2) The state of the prior art: Although there are large number kinase inhibitors known , none of them are claimed or shown to be useful in modulating any or all protein kinases. See Traxler et al.. which suggests such compounds a re in general are at best in the early experimental stage and needs further exploratory studies.

3) The predictability or lack thereof in the art: Applicants have not provided any competent evidence or disclosed tests that are highly predictive for modulation of any or all protein kinases. Pharmacological activity in general is a very unpredictable area. Note that in cases involving physiological activity such as the instant case, "the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved". See *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

4) The amount of direction or guidance present and 5) the presence or absence of working examples: Specification has no working examples for modulating any or all protein kinases and the state of the art is that the effects of agents are unpredictable and at best limited to specific kinases tested..

6) The breadth of the claims: The instant claims embrace any or all protein kinases including non-receptor and receptor protein kinases 7) The quantity of experimentation needed would be an undue burden to one skilled in the pharmaceutical arts since there is inadequate guidance given to the skilled artisan, regarding the pharmaceutical use, for the reasons stated above.

Thus, factors such as "sufficient working examples", "the level of skill in the art" and "predictability", etc. have been demonstrated to be sufficiently lacking in the instant case for the instant method claims. In view of the breadth of the claims, the chemical nature of the invention, the unpredictability of receptor-ligand interactions in general, and the lack of working examples regarding the activity of the claimed compounds towards preventing variety of bacterial infections of the instant claims, one having ordinary skill in the art would have to undergo an undue amount of experimentation to use the instantly claimed invention commensurate in scope with the claims.

Claims 19-37 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating angiogenesis and breast cancer, does not reasonably provide enablement for treating or preventing any or all disorders/disease related to protein kinase generically embraced in claim language. The claim(s) contains subject matter that was not described in the specification in such a way as to enable one skilled in the art of medicinal chemistry - to use the invention. Any claim not specifically rejected is rejected as being dependent on a rejected claim and share the same limitation

The instant claims are drawn to "treating or preventing a protein kinase-related disorder" which include more specific protein tyrosine kinase related disorder such as EGFR, PDGFR, IGFR, flk as well as serine-threonine kinase related disorder. Among the disorders are various autoimmune disorders, hyperprolifertative disorders, inflammatory disorders and various cancers. The scope of the claims includes any or all cancer or any or all proliferative diseases due to protein kinase inhibition including those yet to be discovered as due said mode of action for which there is no enabling disclosure. In addition, the scope of these claims includes treatment of various diseases, which is not adequately enabled solely based on the activity of the compounds provided in the specification at pages 1 and 101-167. The instant compounds are disclosed to have protein kinase inhibitory activity and it is recited that the instant compounds are therefore useful in treating any or all disorders stated above for which applicants provide no competent evidence. It appears that the applicants are asserting that the embraced compounds because of their mode action as kinase inhibitor that would be useful for all sorts of proliferative diseases and cancers, autoimmune diseases, any inflammation or any disease which involve signal trasnduction pathway. However, the applicants have not provided any competent evidence that the instantly disclosed tests are highly predictive for all the uses disclosed and embraced by the claim language for the intended host. Moreover many if not most of diseases such as psoriasis and cancers , autoimmune diseases are very difficult to treat and despite the fact that there are many drugs, which can be used for "inflammatory condition".

The scope of the claims involves various compounds of claim 1 , their prodrugs as well as the thousand of diseases embraced by the terms proliferative disease, cancer, inflammation, and autoimmune disease, or the unknown list of "diseases associated with signal transduction pathways operating through growth factor receptors".

Proliferative disease would include benign tumors, malignant tumors, polyps, lumps, lesions, other pre-cancerous conditions, psoriasis, leukemia, the hyper proliferation of the gastric epithelium caused by the Helicobacter pylori infection of ulcers.

Cancer is just an umbrella term. Tumors vary from those so benign that they are never treated to those so virulent that all present therapy is useless.

Inflammation is a process that can take place in virtually any part of the body. There is a vast range of forms that it can take, causes for the problem, and biochemical pathways that mediate the inflammatory reaction. There is no common mechanism by which all, or even most, inflammations arise. Mediators include bradykinin, serotonin, C3a, C5a, histamine, leukotrienes, cytokines, and many, many others. Accordingly, treatments for inflammation are normally tailored to the particular type of inflammation present, as there is no, and there can be no "magic bullet" against inflammation generally.

The "autoimmune diseases" are a process that can take place in virtually any part of the body. There is a vast range of forms that it can take,' causes for the problem, and biochemical pathways that mediate the inflammatory reaction. There are hundreds

such diseases, which have fundamentally different mechanisms and different underlying causes. Thus, the scope of claims is extremely broad.

No compound has ever been found to treat cancers of all types generally. Since this assertion is contrary to what is known in medicine, proof must be provided that this revolutionary assertion has merits. The existence of such a "compound" is contrary to our present understanding of oncology. Cecil Textbook of Medicine states, "each specific type has unique biologic and clinical features that must be appreciated for proper diagnosis, treatment and study" (see the enclosed article, page 1004). Different types of cancers affect different organs and have different methods of growth and harm to the body. Thus, it is beyond the skill of oncologists today to get an agent to be effective against cancers generally.

The scope of the claims also includes not only treating or preventing any or all disorder mediated by protein kinase for which there is no enabling disclosure. Specification provides no enabling disclosure showing that any or all disease can be prevented with the use of the instant compounds.

"To prevent" actually means *to anticipate* or *counter in advance, to keep from happening etc.* (as per Webster's II Dictionary) and there is no disclosure as to how one skilled in the art can reasonably establish the basis and the type of subject to which the instant compounds can be administered in order to have the "prevention" effect. There is no evidence of record which would enable the skilled artisan in the identification of the people who have the potential of becoming afflicted with any disease in general or the specifically recited disease herein.

Note substantiation of utility and its scope is required when utility is "speculative", "sufficiently unusual" or not provided. See Ex parte Jovanovics, 211 USPQ 907, 909; In re Langer 183 USPQ 288. Also note Hoffman v. Klaus 9 USPQ 2d 1657 and Ex parte Powers 220 USPQ 925 regarding type of testing needed to support in vivo uses.

Next, applicant's attention is drawn to the Revised Interim Utility and Written Description Guidelines, at 64 FR 71427 and 71440 (December 21, 1999) wherein it is emphasized that 'a claimed invention must have a specific and substantial utility'. The disclosure in the instant case is not sufficient to enable the instantly claimed method of preventing solely based on the inhibitory activity disclosed for the compounds. The state of the art is indicative of the requirement for undue experimentation.

See Traxler et al. Ex. Opin. Ther. Patents 7(6): 571-588, 1997. Hasan et al. Expert Opin. Bio. Ther. 1(4): 703-718, 2001(PubMed Abstract provided). Pergram et al. Semin. Oncol. 3 Suppl 11: 29-37, 2002 (PubMed Abstract provided).

MPEP §2164.01(a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was 'filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. In re Wright, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here and undue experimentation will be required to practice Applicants' invention.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the

unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-3, 6-8 and 10-37 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-19 of U.S. Patent No. 6,677,368. Although the conflicting claims are not identical, they are not patentably distinct from each other because the compound, composition and the method of use embraced in instant claims 1-3, 6-8 and10-37 are also embraced in the claims 1-19 of US 6,677,368. Note when instant J = N, R^1 and R^2 are hydrogen, the subject matter embraced in the instant claims are also embraced in the claims 1-19 of US Patent 6,677,368.

Claims 1-3, 6-8 and 10-37 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-25 of U.S. Patent No. 6,642.232. Although the conflicting claims are not identical, they are not patentably distinct from each other because the compound, composition and the method of use embraced in instant claims 1-3, 6-8 and 10-37 are also embraced in the claims 1-25 of US 6,642,232. Note when instant J = N, R^1 and R^2 are hydrogen, Z=

carbamido, the subject matter embraced in the instant claims are also embraced in the claims 1-25 of US Patent 6,642,232.

Claims 1-4, 6-9 and 18 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-13 of U.S. Patent No. 6,635.640. Although the conflicting claims are not identical, they are not patentably distinct from each other because the compound, composition and the method of use embraced in instant claims 1-4, 6-9 and 18 are also embraced in the claims 1-13 of US 6,635,640. Note when instant Q is same as the second choice of Q in the US 6,635,640, and both R^1 and R^2 are hydrogen, the subject matter embraced in the instant claims are also embraced in the claims 1-13 of US Patent 6,635,640.

Claims 1-37 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-40 of U.S. Patent No. 6,486,185. Although the conflicting claims are not identical, they are not patentably distinct from each other because the compound, composition and the method of use embraced in instant claims 1-37 are also embraced in the claims 1-40 of US 6,486,185. Note when instant R^1 and R^2 are hydrogen, the subject matter embraced in the instant claims are also embraced in the claims 1-40 of US Patent 6,486,185.

Claims 1-3, 6-8 and 10-37 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-23 of U.S. Patent No. 6,395,734. Although the conflicting claims are not identical, they are not patentably distinct from each other because the compound, composition and the method of use embraced in instant claims 1-3, 6-8 and 10-37 are also embraced in the

claims 1-23 of US 6,395,734. Note when instant J = N, R^1 and R^2 are hydrogen, the subject matter embraced in the instant claims are also embraced in the claims 1-23 of US Patent 6,395,734.

Claims 1-37 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-29 of U.S. Patent No. 6,316,635. Although the conflicting claims are not identical, they are not patentably distinct from each other because the compound, composition and the method of use embraced in instant claims 1-37 are also embraced in the claims 1-29 of US 6,316,635. Note when instant M = N and/or J = N, R^1 and R^2 are hydrogen, the subject matter embraced in the instant claims are also embraced in the claims 1-29 of US Patent 6,316,635.

Claims 1-37 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-21 of U.S. Patent No. 6,313,158. Although the conflicting claims are not identical, they are not patentably distinct from each other because the compound, composition and the method of use embraced in instant claims 1-37 are also embraced in the claims 1-21 of US 6,313,158. Note when instant J = Nor S or O and R^1 and R^2 are hydrogen, the subject matter embraced in the instant claims are also embraced in the claims 1-21 of US Patent 6,313,158.

Conclusion

Any inquiry concerning this communication from the examiner should be addressed to Venkataraman Balasubramanian (Bala) whose telephone number is (571)

272-0662. The examiner can normally be reached on Monday through Thursday from 8.00 AM to 6.00 PM. The Supervisory Patent Examiner (SPE) of the art unit 1624 is Mukund Shah whose telephone number is (571) 272-0674. If Applicants are unable to reach Mukund Shah within 24-hour period, they may contact James O. Wilson, Acting-SPE of art unit 1624 at 571-272-0661.

The fax phone number for the organization where this application or proceeding is assigned (703) 872-9306. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Venkataraman Balasubramanian

Venkataraman Balasubramanian

9/5/2004